111Equation Chapter 1 Section 1Plasma Clearance

(Renal Clearance of a substance)

- ***Definition:*** It is the volume of plasma that is completely cleared of the amount of substance excreted in urine per minute. If the plasma passing through the kidneys contains 1 mg of a substance in each ml and 1 mg of this substance is also excreted into the urine each minute, then 1 ml / min of the plasma is cleared of the substance.

  Thus, clearance refers to the volume of plasma necessary to supply the amount of substance excreted in urine per unit time.

- ***Calculation:***

  The amount of substance (X) cleared from the plasma / min = C_x X P_x

  Where:

  C_x = Volume of plasma cleared from substance X per minute.

  P_x = Concentration of the substance per 1 ml plasma.

  The amount of substance (X) excreted in urine / min = U_x X V

  Where:

  U_x = Concentration of the substance / ml urine.

  V = Volume of urine / min.

$$C_x \text{ X } P_x = V \text{ X } U_x \qquad C_X = \frac{\mathbf{V \ X \ U_X}}{P_X}$$

This is the equation of Clearance C.

Importance of the determination of plasma clearance

1- Study of the mode of tubular handling **of the different solute in the filtrate**, i.e. either reabsorbed completely e.g glucose, partially reabsorped e.g urea or secreted e.g. creatinine

The following table shows the clearance value of different substances and their significance.

Substance	Tubular Handling	Clearance ml / min
Inulin	Neither reabsorbed or secreted	125
Urea	Partially reabsorbed	< 125
Glucose	Completely reabsorbed	0
PAH	Completely secreted	650
Creatinine	Partially secreted	125-650

2- Measurement of GFR:

By the use of: * Inulin Clearance *Creatinine Clearance

Inulin is a polymer of fructose with a molecular weight of 5200 that is found in dahlia tubers.

- **It possesses the following criteria:**

1) Freely filtered through the glomeruli (not bound to plasma proteins).

So, the concentration of inulin in plasma = concentration of inulin in the filtrate.

2) Not reabsorbed or secreted by the renal tubules.

∴ The amount filtered per minute = The amount excreted in urine per min.

3) Not metabolized.

4) Not stored in the kidneys.

5) Has not effect on filtration rate.

6) Easy to measure in plasma and urine.

- **Steps:** A loading dose of inulin is injected intravenously followed by a sustained infusion to keep the arterial plasma level constant. After inulin has equilibrated with body fluids, urine and plasma samples are collected to determine concentration of inulin in each.
- **Calculations:**

  Quantity of inulin filtered per min = Quantity of inulin excreted in urine per min.

  C_{in} X P_{in} = V X U_{in} ***Where:***

  P_{in} = concentration of inulin in plasma (same concentration as filtrate).

  U_{in} = concentration of inulin in urine.

  V = volume of urine / min.

  C_{in} = volume of filtrate / min. i.e. GFR.

  C_{in} is clearance of inulin which is the volume of plasma that is cleared from the quantity of inulin excreted in urine / min.

$$C_{in} = \frac{U_{in} \times V}{P_{in}}$$

Example:

Inulin is infused in a patient to achieve a steady-state plasma concentration of 2 mg/ml. A urine sample collected during 2 hours has a volume of 120 ml and an inulin concentration of 240 mg/ml. What is the patient's GFR?

$$GFR = \frac{U_{inulin} \times V}{P_{inulin}}$$

$$= \frac{240\ mg/ml \times 1}{2}$$

$$= 120\ ml/min.$$

Creatinine Clearance = C_{cr}.

Creatinine is an endogenous substance that is formed from creatine in muscle.

It possesses the following criteria:

1) Freely filtered.
2) Not reabsorbed.
3) Partially secreted by the renal tubule.

GFR measured by creatinine clearance is slightly higher than GFR value measured with inulin because creatinine is partially secreted .

Endogenous creatinine clearance is easy to measure and is a worthwhile index of renal function.

GFR can be estimated from the formula of Cockcroft and Gault which incorporates age,sex and weight to estimate creatinine clearance from plasma creatinine level without any urinary measurement.

$$GFR = \frac{(140 - Age) \times Weight\ (Kg)}{P_{cr} \times 72}$$

For woman, the estimated GFR is multiplied by 0.85 because muscle mass is less.

3- Measurement of the renal plasma flow:

The substance used is PAH, because: PAH: Para-amino Hippuric acid

- Is freely filtered by the glomerulus.

-Is completely secreted from the peritubular capillary blood into the tubular lumen in a single circulation through the kidney.

∴The amount of PAH in plasma of the renal artery = The amount of PAH excreted in urine.

- Renal plasma flow can be calculated from clearance of PAH." C_{PAH}"

$$C_{\text{PAH}} = \frac{U_{\text{PAH}} \text{ X } \text{V}}{P_{\text{PAH}}}$$

However, the extraction ratio of PAH is 90% i.e. only 90% of PAH in renal arterial blood is removed in a single circulation through the kidney. Therefore C_{PAH} provides the effective renal plasma flow (ERPF)

$$\text{ERPF} = \frac{U_{\text{PAH}} \text{ X } \text{V}}{P_{\text{PAH}}}$$

Actual renal plasma flow (RPF) = ERPF / extraction ratio

Renal blood flow = RPF /1 - HV

(HV = Hematocrit Value)

Problem:

Concentration of PAHA in urine (U_{PAH}) = 14 mg/ml

Urine flow (V) = 0.9 ml/min

Concentration of PAHA in plasma (P_{PAH}) = 0.02 mg/ml

Extraction ratio = 0.9

HV = 45%

Calculate the RBF

$$\textbf{ERPF} = \frac{\textbf{14 x 0.9}}{\textbf{0.02}} = \textbf{630 ml/min.}$$

$$\textbf{RPF} = \textbf{630 / 0.9} = \textbf{700 ml/min.}$$

$$\mathbf{RBF} = \frac{\mathbf{700}}{\mathbf{1 - 0.45}} ¿ \mathbf{1273\ ml/min}.$$

4- Calculation of filtration fraction:

Filtration fraction is the ratio of the GFR to the renal plasma flow. GFR is determined by inulin clearance. RPF is determined by PAH clearance.

If RPF = 700 ml/min GFR= 125

$$F.F. = \frac{\mathbf{125}}{\mathbf{700}} = 0.\mathbf{19}$$

ml/min

Normal value = 0.16 - 0.20

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